

Aventis Pharmaceuticals



February 12, 2002

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Via fax and UPS

Dockets Management Branch (HFA-305)
Food and Drug Administration
5630 Fishers Lane, Room 1061
Rockville, MD 20852

Re: Docket No. 01D-0510

Draft Guidance for Industry on Integration of Dose-Counting Mechanisms into MDI Drug Products [66FR 64045, December 11, 2001]

Dear Sir/Madam:

Aventis Pharmaceuticals Inc would like to thank you for the opportunity to comment on the above-referenced draft guidance entitled "Integration of Dose-Counting Mechanisms into MDI Drug Products". The document makes recommendations to manufacturers to incorporate dose-counters into metered dose inhalers (MDIs) being developed for the treatment of lung diseases. We offer the following comments/clarification for your consideration.

I. INTRODUCTION

Page 1 – 1st sentence

This guidance is intended to assist manufacturers who are developing or plan to develop drug products for oral inhalation using metered dose inhalers (MDIs).

We understand this guidance would apply equally to delivery of any drug product using this route and device type, and would not be restricted to MDIs being developed for the treatment of lung diseases.

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II. BACKGROUND

Page 2 – Last paragraph – Last sentence

Nasally delivered drugs are more typically intended to treat bothersome, but non-life threatening, conditions.

We agree that non-life threatening nasal products do not require a dose-counter but it might become necessary for life threatening conditions.

III. INTEGRATION OF DOSE-COUNTING MECHANISMS INTO MDI PRODUCTS UNDER DEVELOPMENT

A. General Recommendations

Page 2 – 1st paragraph - 2nd sentence

Dose-counters should provide, either through a direct numeric count or color coding, a clear indication of when an MDI is approaching the end of its recommended number of actuations as well as when it has reached or exceeded that number.

We suggest that when color coding is used, consideration is given to use a harmonized color to indicate that the end of the recommended number of actuations is approaching, namely red.

Page 3 – 2nd paragraph – Last sentence

In such cases, manufacturers are encouraged to commit to developing an integrated dose-counter in the postmarketing period.

If this is a requirement, it should state this is required in the postmarketing period. We suggest rephrasing the sentence as follows: “*In such cases, manufacturers are required to commit to developing an integrated dose-counter in the postmarketing period. The absence of a dose-counter at submission time will not cause the withholding of the product approval, when a commitment is provided.*”

B. Reliability Issues


Page 3 – Last sentence

The reliability of dose-counters should be established during development under in-vitro testing (simulating use and potential abuse), as well as in clinical use studies that are designed and conducted to obtain information on the technical function and the perceived utility for patients of the counters in actual use.

We suggest that clinical use studies could be incorporated into early phase clinical studies instead of conducting separate clinical use studies to obtain information on dose-counter technical function and utility. Phase III clinical trials should have the dose-counting mechanism present.

On behalf of Aventis Pharmaceuticals Inc we appreciate the opportunity to comment on the draft guidance for industry on Integration of Dose-Counting Mechanisms into MDI Drug Products, and thank you for your consideration.

Sincerely,

A handwritten signature in black ink, appearing to read "Caffé", with a stylized, flowing script.

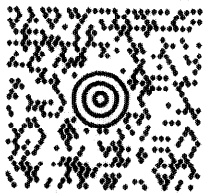
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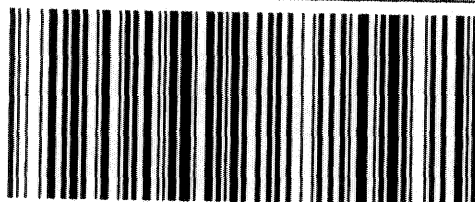
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